

WHAT IS CLAIMED IS:

1. A method for the assessment of the responsiveness of a cancer patient to antifolate-containing chemotherapy, the method comprising the step of searching for a mutation or mutations in a gene associated with folate metabolism or uptake in cells derived from the patient.

2. The method of claim 1, wherein said the human gene associated with folate metabolism or uptake is the reduced folate carrier (RFC) gene.

3. The method of claim 1, wherein said gene associated with folate metabolism or uptake is selected from the group consisting of the following human genes: dihydrofolate reductase (DHFR), folylpoly γ -glutamate synthetase (FPGS), folylpoly γ -glutamate hydrolase (FPGH), glycylamide ribonucleotide transformylase (GARTF), phosphoribosylamino-imidazole-carboxamide transformylase (AICARTF), thymidylate synthase (TS), Multidrug resistance 1 (MDR1), multidrug resistance protein 1 (MRP1), multidrug resistance protein 2 (MRP2) gene and multidrug resistance protein 3 (MRP3).

4. The method of claim 1, wherein said cells are tumor cells.

5. The method of claim 1, wherein said cells are non-tumor cells.

6. The method of claim 1, further comprising the step of evaluating an effect of mutation or mutations found in said gene on

antifolate and reduced folate uptake or metabolism in tumor cells of the patient.

7. The method of claim 2, further comprising the step of evaluating an effect of mutation or mutations found in said reduced folate carrier (RFC) gene on antifolate and reduced folate uptake in tumor cells of the patient.

8. The method of claim 7, wherein said step of evaluating an effect of said mutation or mutations found in said reduced folate carrier (RFC) gene on said antifolate and said reduced folate uptake in said tumor cells of the patient is effected by previous knowledge regarding said mutation or mutations.

9. The method of claim 7, wherein said step of evaluating an effect of said mutation or mutations found in said reduced folate carrier (RFC) gene on said antifolate and said reduced folate uptake in said tumor cells of the patient is effected by evaluating the effect on uptake of said antifolate and said reduced folate by cells expressing a mutated reduced folate carrier protein encoded by a polynucleotide harboring said mutation or mutations.

10. The method of claim 1, wherein said step of searching for said mutation or mutations in said gene in said cells derived from the patient is effected by a single strand conformational polymorphism (SSCP) technique.

11. The method of claim 10, wherein said single strand conformational polymorphism technique is selected from the group consisting of cDNA-SSCP and genomic DNA-SSCP.

12. The method of claim 1, wherein said step of searching for said mutation or mutations in said gene in said cells derived from the patient is effected, at least in part, by a technique selected from the group consisting of nucleic acid sequencing, polymerase chain reaction, ligase chain reaction, self-sustained synthetic reaction, Q β -Replicase, cycling probe reaction, branched DNA, restriction fragment length polymorphism analysis, mismatch chemical cleavage, heteroduplex analysis, allele-specific oligonucleotides, denaturing gradient gel electrophoresis, constant denaturant gel electrophoresis, temperature gradient gel electrophoresis and dideoxy fingerprinting.

13. A method for the assessment of the responsiveness of tumor cells to antifolate-containing chemotherapy, the method comprising the step of searching for a mutation or mutations in the tumor cells.

14. The method of claim 13, wherein said gene associated with folate metabolism or uptake is reduced folate carrier (RFC) gene.

15. The method of claim 13, wherein said gene associated with folate metabolism or uptake is selected from the group consisting of dihydrofolate reductase (DHFR) gene, folylpoly γ -glutamate synthetase (FPGS) gene, folylpoly γ -glutamate hydrolase (FPGH) gene, glycylamide ribonucleotide transformylase (GARTF) gene, phosphoribosylamino-imidazole-carboxamide transformylase (AICARTF) gene, thymidylate synthase (TS) gene, multidrug resistance protein 1 (MDR1) gene, multidrug resistance protein 1 (MRP1) gene, multidrug resistance protein 2 (MRP2) gene and multidrug resistance protein 3 (MRP3) gene.

16. The method of claim 13, further comprising the step of evaluating an effect of mutation or mutations found in said gene on antifolate and reduced folate uptake or metabolism in tumor cells of the patient.

17. The method of claim 14, further comprising the step of evaluating an effect of mutation or mutations found in said reduced folate carrier (RFC) gene on antifolate and reduced folate uptake in said tumor cells.

18. The method of claim 16, wherein said step of evaluating an effect of said mutation or mutations found in said gene on said antifolate and said reduced folate uptake or metabolism in said tumor cells is effected by previous knowledge regarding said mutation or mutations.

19. The method of claim 17, wherein said step of evaluating an effect of said mutation or mutations found in said reduced folate carrier (RFC) gene on said antifolate and said reduced folate uptake in said tumor cells is effected by previous knowledge regarding said mutation or mutations.

20. The method of claim 17, wherein said step of evaluating an effect of said mutation or mutations found in said reduced folate carrier (RFC) gene on said antifolate and said reduced folate uptake in said tumor cells is effected by evaluating the effect on uptake of said antifolate and said reduced folate by cells expressing a mutated reduced folate carrier protein encoded by a polynucleotide harboring said mutation or mutations.

21. The method of claim 13, wherein said step of searching for said mutation or mutations in said gene in said tumor cells is effected by a single strand conformational polymorphism (SSCP) technique.

22. The method of claim 21, wherein said single strand conformational polymorphism technique is selected from the group consisting of cDNA-SSCP and genomic DNA-SSCP.

23. The method of claim 13, wherein said step of searching for said mutation or mutations in said gene in said cells derived from the patient is effected, at least in part, by a technique selected from the group consisting of nucleic acid sequencing, polymerase chain reaction, ligase chain reaction, self-sustained synthetic reaction, Q β -Replicase, cycling probe reaction, branched DNA, restriction fragment length polymorphism analysis, mismatch chemical cleavage, heteroduplex analysis, allele-specific oligonucleotides, denaturing gradient gel electrophoresis, constant denaturant gel electrophoresis, temperature gradient gel electrophoresis and dideoxy fingerprinting.

24. A kit for assessing a responsiveness of a cancer patient to antifolate chemotherapy, the kit comprising a holder for holding at least one container containing oligonucleotides capable of amplifying at least one fragment of a gene associated with folate metabolism or uptake.

25. The kit of claim 24, wherein said gene associated with folate metabolism or uptake is reduced folate carrier (RFC) gene.

26. The kit of claim 24, wherein said gene associated with folate metabolism or uptake is selected from the group consisting of dihydrofolate reductase (DHFR) gene, folylpolyglutamate synthetase

(FPGS) gene, folylpoly γ -glutamate hydrolase (FPGH) gene, glycinamide ribonucleotide transformylase (GARTF) gene, phosphoribosylamino-imidazole-carboxamide transformylase (AICARTF) gene, thymidylate synthase (TS) gene, multidrug resistance protein 1 (MDR1) gene, multidrug resistance protein 1 (MRP1) gene, multidrug resistance protein 2 (MRP2) gene and multidrug resistance protein 3 (MRP3) gene.

27. The kit of claim 24, further comprising a container containing a DNA polymerase enzyme.

28. The kit of claim 24, further comprising a container containing a reverse transcriptase enzyme.

29. The kit of claim 24, further comprising a container containing a mixture of dNTPs.

30. The kit of claim 24, further comprising a container containing a concentrated polymerase chain reaction buffer.

31. The kit of claim 24, wherein said oligonucleotides are selected from the group of oligonucleotides identified by SEQ ID NOs:1-20.

32. The kit of claim 24, wherein at least one of said oligonucleotides includes at least one nucleotide analog.

33. The kit of claim 24, wherein at least one of said oligonucleotides includes a labeling moiety.

34. The kit of claim 24, further comprising at least one precast gel for executing single strand conformational polymorphism.

35. The kit of claim 24, further comprising at least one container containing reagents for detection of electrophoresed nucleic acids.